

**METHOD OF INHIBITING OPIOID TOLERANCE WITH CHIMERIC HYBRID
ANALGESICS**

AMENDMENT NO 1 TO CLAIMS

(once amended) 1. A method of inhibiting the development of opioid tolerance by clinically administering a clinically combination of a pharmacologically active form of substance P with morphine in a chimeric hybrid molecule wherein morphine, chemically modified and covalently linked through its 6'OH group, comprises a cyclic alkaloid moiety which binds as an agonist to a mammalian ~~or human~~ mu (μ) opioid receptor; and wherein a pharmacologically active C-terminal substance P fragment, chemically modified and covalently linked through its free NH₂ group, comprises a peptide moiety which binds as an agonist to a mammalian/~~human~~ substance P receptor; and wherein a compact, but flexible, molecular hinge covalently cross links morphine through its 6'OH group to the free NH₂ group of the substance P receptor agonist moiety, so as to allow both the mu (μ) opioid receptor and the substance P receptor agonist moieties to activate their respective receptors simultaneously and independently.